POLYPHARMACY

UTHealth

The University of Texas
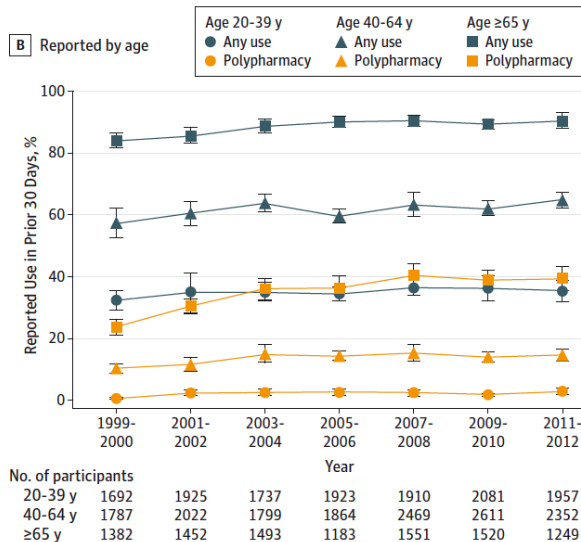**Health Science Center at Houston**

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Geriatric and Palliative Medicine
UTHealth Medical School

Medication-related problems

- Almost 1/5 of older persons take 10 medications in any given week
- 10-30% of older adults experience an adverse drug reaction each year
- 20% of older outpatients takes an inappropriate drug every year
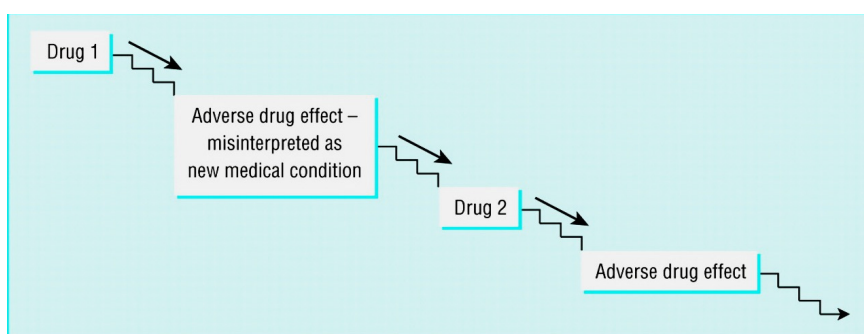- 4% older adults are exposed to a potentially severe drug-drug interaction

Slone Survey, 2010.
Qato, JAMA 2008;300:303-9.
Hines, Am J Geriatr Pharmacother 2011; 9: 364-77.

Trends in drugs use: NHANES

	Age 20-39 y	Age 40-64 y	Age ≥65 y
B Reported by age	● Any use	▲ Any use	■ Any use
	● Polypharmacy	▲ Polypharmacy	■ Polypharmacy

No. of participants	1999-2000	2001-2002	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012
20-39 y	1692	1925	1737	1923	1910	2081	1957
40-64 y	1787	2022	1799	1864	2469	2611	2352
≥65 y	1382	1452	1493	1183	1551	1520	1249

Kantor ED. JAMA. 2015;314(17):1818-1831.

The prescribing cascade

Drug 1 →

Adverse drug effect – misinterpreted as new medical condition

Drug 2 →

Adverse drug effect

- **Adverse drug reactions**
- **Poor adherence**
- **Increased cost**
- **Use of inappropriate medications**
- **Geriatric syndromes**
- **Undertreatment**

Shelton, P, et al. *Drugs & Aging.* 2000; 16: 437-450.
Delafuente, JC. *Crit Rev Hem Oncol.* 2003; 48: 133-143.

Rochon, P. A et al. *BMJ* 1997;315:1096-1099.
Steinman MA, et al. *J Am Geriatr Soc* 2006; 54:1516-1523.

Defining polypharmacy based on outcomes

Falls (≥ 2)

Frailty (≥ 4)

2.0 (12.7%, 97.3%)

5.0 (44.5%, 75.7%)
5.5 (59.2%, 73.0%)

7.0 (66.2%, 64.9%)

AUC: 66.2%

10.0 (85.5%, 24.3%)

Sensitivity (%)

Specificity (%)

2.0 (12.5%, 95.0%)

5.0 (44.9%, 77.5%)

7.0 (67.0%, 70.0%)*

10.0 (87.2%, 37.5%)

AUC: 71.1%

Sensitivity (%)

Specificity (%)
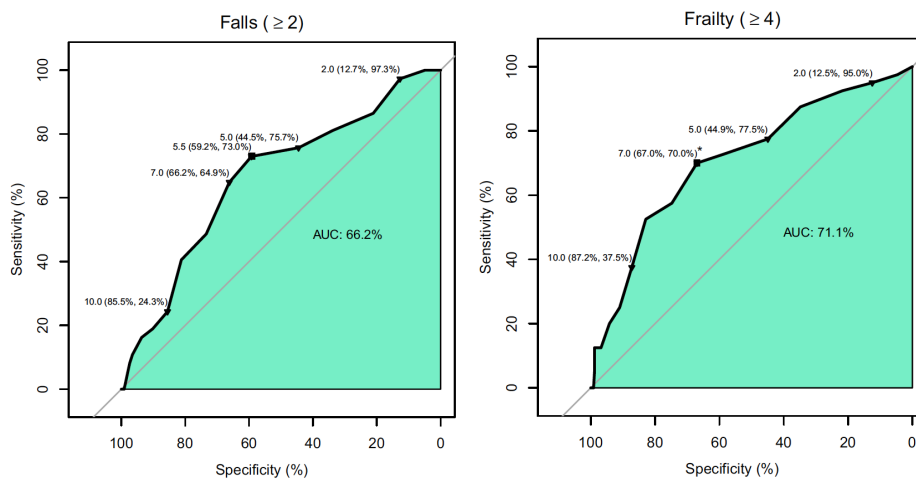
Turner JP. Support Care Cancer, epub Oct 2015.

Polypharmacy and cancer

- Prevalence of ≥5 meds
  - 13% to 92% in general elderly populations
  - 21% to 80% in cancer
- Median number of drugs in older cancer patients ranges 5-9.1
- Higher use in advanced cancer
- Associated factors in cancer: higher comorbidity, worse ECOG PS, frailty, poor physical function

Lees J and Chan A., Lancet Oncol, 2011.
Maggiore R, Gross C, Hurria A. Oncologist, 2010.
Turner JP et al. Support Care Cancer, 2014.
Kierner KA Support Care Cancer Nov 2015.

Prithviraj, J Geriatr Oncol, 2012.
Hamaker, Breast, 2014.
Rocco, BMC Surgery, 2013.
Badgwell, J Surg Oncol, 2013.

Evidence for the harms of polypharmacy

- All observational studies, mostly cohort and longitudinal cohort, some case-control
  - Mixed results, some with poor adjustment for comorbidity
- Increasing med number associated with
  - Falls and dizziness
  - Adverse drug events
  - Hospitalizations
- Message: too much heterogeneity in definition of polypharmacy and outcomes, need to test discontinuation, focus on high risk drugs

Fried T, et al. *J Am Geriatr Soc*. 2014;62:2261-2272.

Polypharmacy and Outcomes in Cancer

- OR (unadj) 6.38 (1.99-23.47) for grade 3-4 toxicity in 73 patients with metastatic breast cancer

- OR 16.65 (9.12-30.58) for postop complications in 449 patients with breast cancer

- OR 2.45 (1.09-5.49) for prolonged length of stay after abdominal cancer surgery in 111 patients

- Not associated with early d/c of palliative chemo in 98 patients ≥65 years

- Taking >6 meds/day associated with decreased OS in 83 pts with ovarian cancer

Hamaker, Breast, 2014.
Rocco, BMC Surgery, 2013.
Badgwell, J Surg Oncol, 2013.

Kim. Support Care Cancer. 2013 Nov 28.
Freyer G. Ann Oncol. 2005;16(11):1795-1800.

Strategies to mitigate polypharmacy

- Avoid high risk / low benefit meds >> "inappropriate" drugs
- Avoid drugs that lead to adverse reactions
- Approach all prescribing with deprescribing in mind

Inappropriate medication use: Beers criteria

- Developed by consensus using Delphi method in 1991, with updates in 1997, 2003, 2012, 2015
- 53 medications/drugs classes that are inappropriate
- Criteria variably associated with adverse drug events, hospitalization, mortality
- Individual drugs associated with delirium, GI bleeding, falls, fractures

Fick DM et al. Arch Intern Med. 2003;163:2716-24.
Lund BC et al . Ann Pharmacother 2011;45:1363-70.
AGS Beers Panel. J Amer Geriatr Soc 2012, 2015.

Inappropriate Medication Use in Cancer

- Registry study of patients 70+, those with cancer had twice the risk of use of z-type sedatives, benzodiazepines, and opioids
- Oncology ACE unit intervention to decrease inappropriate meds included 47 patients, mean age 73.5, 21% taking at least one Beers drug
- 117 patients, mean age 74.6, 41% took at least one Beers drug
- Nightingale et al >>> 10:30 am session

Ineke Neutel C, Pharmacoepi Drug Safety, 2012.
Flood, Am J Geriatr Pharmacother, 2009.
Prithviraj, J Geriatr Oncol, 2012.

Inappropriate medications and outcomes in cancer

- 500 patients 65+ receiving chemotherapy, 29% getting Beers drugs
  - No association with grade 3-5 chemotoxicity, OR 0.97 (0.66-1.43)
  - No association with hospitalizations during chemo, OR 1.01 (0.64-1.61)
- 1595 women with breast cancer getting chemo, 21.3% on a high-risk subset of Beers
  - No association with ER visits, hospitalization or death during chemo, OR 1.23 (0.97-1.57)

Maggiore R et al for CARG. J Am Geriatr Soc 62:1505–1512, 2014.
Karuturi M. ASCO abstract 2015.

Screening Tool of Older Peoples' Prescriptions

- 80 if/then indicators for drugs that are not appropriate for people 65 and older
- Consistently and significantly associated with adverse drug events
- Significant improvement in inappropriate meds that persisted for 6 months
- Significant reduction in adverse drug reactions applied within 72 hrs of admission

O'Mahoney D, et al. Age Ageing 2014;0:1-6.

Anticholinergic Drugs

- Drugs with high serum anticholinergic activity
- Multiple scales to rate drugs, suggest less anticholinergic alternatives

Table 3. Regression Model Predicting Association Between Anticholinergic Scales and Hospital Admission, Falls-Related Hospitalization, Length of Stay (LOS), and General Practitioner (GP) Visits

Scale	Hospital Admissions	Falls-Related Hospitalization	LOS	GP Visits
	Incident Rate Ratio (Confidence Interval)			
Carnahan, United States, 2006[8]	1.280 (1.258–1.303)	1.212 (1.172–1.255)	1.315 (1.291–1.339)	1.092 (1.089–1.095)
Ancelin, France, 2006[6]	1.191 (1.169–1.214)	1.172 (1.131–1.214)	1.248 (1.222–1.273)	1.056 (1.053–1.060)
Han, United States, 2008[10]	1.234 (1.211–1.257)	1.205 (1.159–1.254)	1.272 (1.248–1.298)	1.087 (1.083–1.090)
Rudolph, United States, 2008[11]	1.244 (1.215–1.274)	1.209 (1.150–1.271)	1.308 (1.276–1.341)	1.093 (1.089–1.098)
Chew, United States, 2008[5]	1.138 (1.117–1.159)	1.141 (1.095–1.190)	1.235 (1.211–1.260)	1.077 (1.074–1.081)
Boustani, United States, 2008[7]	1.231 (1.209–1.253)	1.201 (1.158–1.245)	1.295 (1.271–1.319)	1.080 (1.077–1.083)
Sittironnarit, Australia, 2011[12]	1.208 (1.185–1.231)	1.221 (1.172–1.273)	1.276 (1.250–1.301)	1.079 (1.076–1.083)
Ehrt, Norway, 2010[9]	1.144 (1.126–1.163)	1.090 (1.055–1.127)	1.194 (1.174–1.215)	1.055 (1.052–1.057)
Hilmer, United States, 2007[19]	1.364 (1.310–1.420)	1.591 (1.458–1.736)	1.500 (1.439–1.563)	1.261 (1.252–1.270)

P-value (<.001) determined using logistic regression model that included age, ethnicity, polypharmacy, chronic disease score, and sex.

Salahudeen MS, Hilmer SN, Nishtala PS. J Am Geriatr Soc 63:85–90, 2015.

Drug-induced ER admission in older persons

- 2007-2009 data used to estimate:
  - Frequency and rates of hospitalization after ER visits for ADRs in older adults (> 65 years old)
- Nearly half were in adults > 80 years
- Nearly 2/3 were due to unintentional overdose
- Beers drugs were only 1.2%
- Four medications/medication classes were implicated

Budnitz, NEJM 2011;365:2002-2012.
Juurlink. JAMA 2003;289:1652-58.

Drug-induced ER admission in older persons
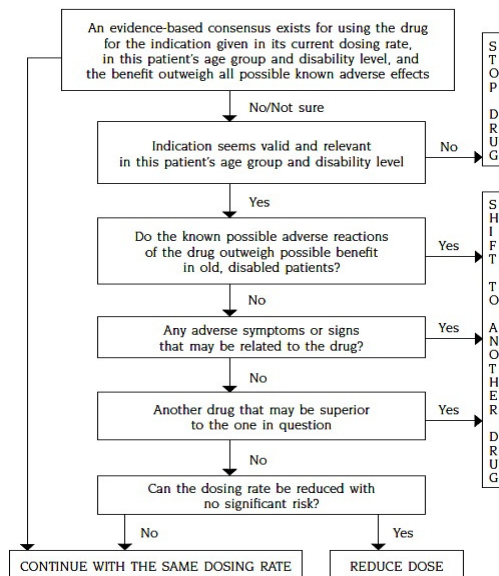
% Hospital Admissions
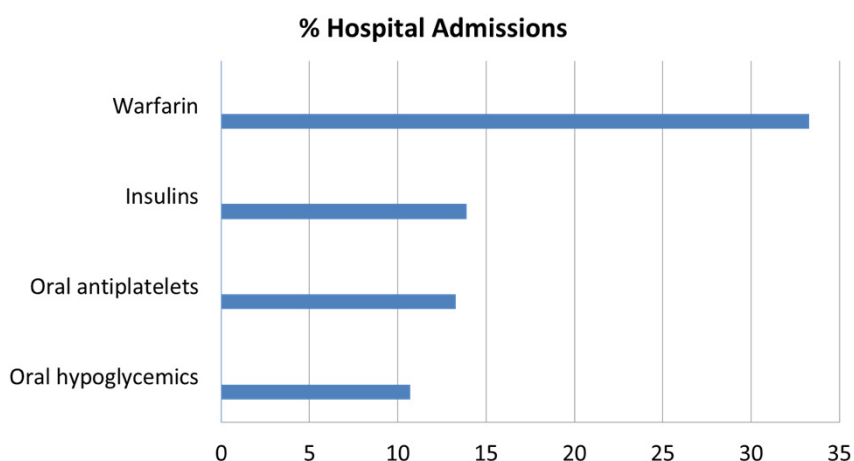
Budnitz, NEJM 2011;365:2002-2012.

GP-GP Algorithm

- Developed for nursing home use
- 119 GP-GP, 71 control
- 2.8 meds/pt stopped
- 18% D/C failure
- Reduced mortality, rehospitalization, and cost

Garfinkel D. *Arch Intern Med.* 2010; 170 :1648-1654.

An evidence-based consensus exists for using the drug for the indication given in its current dosing rate, in this patient's age group and disability level, and the benefit outweigh all possible known adverse effects

No/Not sure

Indication seems valid and relevant in this patient's age group and disability level — No — STOP DRUG

Yes

Do the known possible adverse reactions of the drug outweigh possible benefit in old, disabled patients? — Yes

No

Any adverse symptoms or signs that may be related to the drug? — Yes — SHIFT TO ANOTHER DRUG

No

Another drug that may be superior to the one in question — Yes

No

Can the dosing rate be reduced with no significant risk?

No — CONTINUE WITH THE SAME DOSING RATE   Yes — REDUCE DOSE

Medication Review

1. Does every medication match a known medical problem or chronic condition?
   - Any deficiencies?
   - Any duplications?
2. What are the categories of drugs and their mechanism of action?
3. What is the patient's creatinine clearance using the Cockcroft Gault equation?
4. Are the dosages appropriate for each medication for the patient's age, renal, or liver function?
5. Are there red flags for potential drug-drug or drug-disease interactions or medication complications?
6. What are the patient's current complaints or presenting problems, including onset and duration?
7. Could a medication related problem be responsible?
   - Any recent additions or deletions?
   - Any correlation with the timing of the medication and the presenting symptoms?
8. What are the relevant medication-related issues? (ie, drug interactions, side effects, administration)
9. Can the regimen be simplified?

George CJ, Jacobs LG. Geriatrics medication management rounds: a novel approach to teaching rational prescribing with the use of the medication screening questionnaire. J Am Geriatr Soc. 2011;59:138-42.

The Process of Deprescribing

1. Ascertain that all drugs the patient is currently taking and the reasons for each one.

2. Consider overall risk of drug-induced harm in individual patients in determining the required intensity of deprescribing intervention.

3. Assess each drug for its eligibility to be discontinued.

4. Prioritize drugs for discontinuation.

5. Implement and monitor drug discontinuation regimen.

Scott et al. JAMA Internal Medicine 2015

Deprescribing in advanced disease
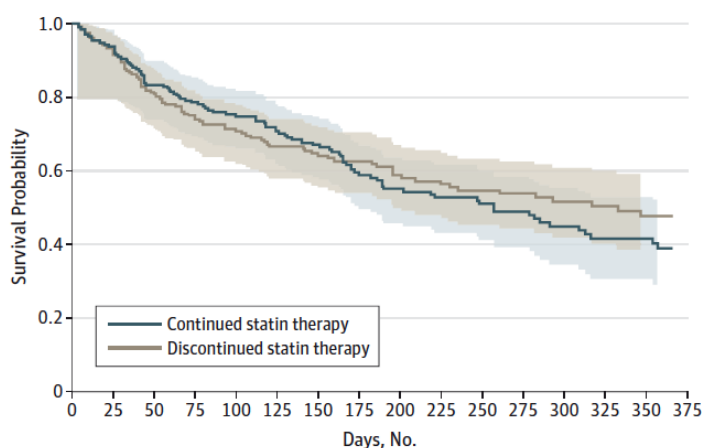
Kutner et al. JAMA Internal Medicine. 2015

No. at risk							
Continued statin therapy	192	149	105	64	47	32	21
Discontinued statin therapy	189	135	93	68	52	36	26

Practical recommendations for older patients with cancer

- Mitigate the chances of harmful drug exposure

- Recognize that data for and against medication safety is often extrapolated or from observational studies

- Understand that many essential supportive care drugs are considered inappropriate in the elderly

Key Points

- Older patients are the highest users of medication and are the most vulnerable to the problems caused by medications.

- Keep in mind that many drugs that lead to hospital admissions are actually not on any lists of drugs to avoid (warfarin, antiplatelet agents, hypoglycemics, digoxin, ACE inhibitors).

- The best strategy is to pick a tool and stick with it, or focus on reducing medication number?

Thank you

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